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PPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
09/855,750	05/16/2001	Madhavan Nampoothiri K.	32301WD1181	8888
759	90 11/03/2004		EXAM	INER
SMITH GAMBRELL & RUSSELL, L.L.P.			STEADMAN, DAVID J	
Suite 800 1850 M Street, I	N W		ART UNIT	PAPER NUMBER
Washington, DC 20036			1652	
			DATE MAILED: 11/03/2004	1

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s)
	09/855,750	NAMPOOTHIRI K. ET AL.
Office Action Summary	Examiner	Art Unit
	David J Steadman	1652
The MAILING DATE of this communication app	pears on the cover sheet with the c	correspondence address
A SHORTENED STATUTORY PERIOD FOR REPL THE MAILING DATE OF THIS COMMUNICATION.  - Extensions of time may be available under the provisions of 37 CFR 1.1 after SIX (6) MONTHS from the mailing date of this communication.  - If the period for reply specified above is less than thirty (30) days, a repl 1 fl NO period for reply is specified above, the maximum statutory period Failure to reply within the set or extended period for reply will, by statute Any reply received by the Office later than three months after the mailin earned patent term adjustment. See 37 CFR 1.704(b).	136(a). In no event, however, may a reply be till by within the statutory minimum of thirty (30) day will apply and will expire SIX (6) MONTHS from a cause the application to become ABANDONE	nely filed ys will be considered timely. I the mailing date of this communication. ED (35 U.S.C. § 133).
Status		
1) Responsive to communication(s) filed on 31 A	ugust 2004.	
,—	s action is non-final.	
3) Since this application is in condition for allowa		
closed in accordance with the practice under	Ex parte Quayle, 1935 C.D. 11, 4	53 O.G. 213.
Disposition of Claims		
4)	wn from consideration. re allowed. d.	
Application Papers	1	
9)⊠ The specification is objected to by the Examin		_
10)⊠ The drawing(s) filed on 16 May 2001 is/are: a		
Applicant may not request that any objection to the Replacement drawing sheet(s) including the correct		
11) The oath or declaration is objected to by the E		
Priority under 35 U.S.C. § 119		
12) Acknowledgment is made of a claim for foreign a) All b) Some * c) None of:  1. Certified copies of the priority document 2. Certified copies of the priority document 3. Copies of the certified copies of the priority document application from the International Bureat* See the attached detailed Office action for a list	its have been received. Its have been received in Applica prity documents have been receiv au (PCT Rule 17.2(a)).	tion No. <u>09/577,848</u> . ved in this National Stage
Attachment(s)  1) Notice of References Cited (PTO-892) 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08 Paper No(s)/Mail Date	4) Interview Summar Paper No(s)/Mail I 5) Notice of Informal 6) Other:	

Art Unit: 1652

#### **DETAILED ACTION**

## Status of the Application

- [1] Claims 25-27 and 29-46 are pending in the application.
- [2] Applicants' amendment to the claims, filed August 31, 2004, is acknowledged.

  This listing of the claims replaces all prior versions and listings of the claims.
- [3] It is noted that the text of canceled claim 47 recites additional text that was not present in claim 47 of the amendment filed May 12, 2003.
- [4] Applicants' arguments filed on August 31, 2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [5] The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.
- [6] The indicated allowability of claims 30, 36-39, 42, 45-46 is withdrawn in view of the new rejections stated below.

## **Priority**

[7] Applicants' claim to domestic priority under 35 USC 120 to US non-provisional application 09/577,848, filed May 25, 2000, is acknowledged. Applicants' claim to foreign priority under 35 USC 119(a)-(d) to German application 100 21 831.8, filed March 04, 2000, is acknowledged. The German priority document is filed in application 09/577,848.

Art Unit: 1652

#### Oath/Declaration

[8] It is noted that the first paragraph of the specification states the instant application claims priority under 35 U.S.C. 119 to German Patent Application 10021831.8, filed May 04, 2000, while the Declaration filed August 31, 2001 states the instant application claims priority to the same German Patent Application with a filing date of March 04, 2000. Clarification is requested and, if necessary, the appropriate correction is required.

## Specification/Informalities

- [9] The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: --fadD15 Gene Encoding An Acyl-CoA Synthase--
- [10] The specification is objected to as being confusing in that SEQ ID NO:1 does not encode the polypeptide of SEQ ID NO:2 as disclosed in the specification. The codon encoding the first amino acid of SEQ ID NO:2, a methionine, is the triplet TTG. Also, the sequence listing for SEQ ID NO:1 shows that the first encoded amino acid, a methionine, is encoded by the triplet TTG. However, it is well known in the art that the codon TTG encodes a leucine and not a methionine. Clarification is requested.

#### Claim Objection

Art Unit: 1652

[11] Claim 46 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 31. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

## Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

- [12] Claim(s) 30, 42, and 45-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
- [a] Claims 30, 42, and 45 are confusing in that it appears from claims 30 and 42 that Deposit DSM 13249 is a vector. However, from the specification, it appears that Deposit DSM 13249 is a host cell (see pp. 18 and 25-26 of the specification). It is suggested that applicants clarify the meaning of the claims.
- [b] Claim 46 is unclear as to the intended acyl-CoA synthase that is encoded by the degenerate variant of nucleotides 247-2103 of SEQ ID NO:1. From the specification it appears that nucleotides 247-2103 of SEQ ID NO:1 encode the polypeptide of SEQ ID NO:2 (see SEQ ID NO:1 and 2 of the sequence listing). Thus, a degenerate variant of SEQ ID NO:1 would necessarily encode SEQ ID NO:2. However, it is not clear from the

Art Unit: 1652

claims and specification as to whether this is the case, *i.e.*, that the scope of degenerate variants encoded by nucleotides 247 to 2103 of SEQ ID NO:1 is limited to encoding SEQ ID NO:2. The examiner has interpreted the claim as meaning the degenerate variant encodes the acyl-CoA synthase of SEQ ID NO:2. Clarification of the intended encoded acyl-CoA synthase is requested.

## Claim Rejection - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[13] Claim(s) 36-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 36 (claim 37 dependent therefrom) is drawn to a genus of isolated polynucleotides consisting of at least 15 consecutive nucleotides of SEQ ID NO:1 or the complement thereof, wherein the polynucleotide is a PCR primer for synthesis of an acyl-CoA synthase-encoding nucleic acid. Claim 37 (claim 38 dependent therefrom) is drawn to a genus of isolated polynucleotides consisting of at least 15 consecutive nucleotides of SEQ ID NO:1 or the complement thereof, wherein the polynucleotide is a hybridization probe for isolation of an acyl-CoA synthase-encoding nucleic acid. Claims

Art Unit: 1652

36-37 recite the transitional phrase "consisting of." However, in view of the inclusion of "at least" in claims 36-37, the recited genus of polynucleotides is not limited to a fragment of SEQ ID NO:1, but instead encompasses any polynucleotide with at least 15 nucleotides of SEQ ID NO:1 and any additional sequence. In accordance with MPEP 2111. the claims have been interpreted as encompassing not only nucleic acid fragments, but also full-length polynucleotides. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single representative species of the genus of claimed isolated polynucleotides, i.e., SEQ ID NO:1. The specification fails to describe any additional representative species of the claimed genus. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely

Art Unit: 1652

variant species cannot be achieved by disclosing only one species within the genus". In the instant case, the recited genus of polynucleotides encompasses species that are widely variant in structure. As such, the single representative species of the genus of polynucleotides is insufficient to be representative of the attributes and features of *all* species encompassed by the claimed genus. Given the lack of description of a representative number of polynucleotides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[14] Claim(s) 36-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:1, does not reasonably provide enablement for the broad scope of polynucleotides consisting of *at least* 15 consecutive nucleotides of SEQ ID NO:1 for use as PCR primers or hybridization probes as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The

Application/Control Number: 03/030,73

Art Unit: 1652

existence of working examples; and (H) The quantity of experimentation needed to

Page 8

make or use the invention based on the content of the disclosure. See MPEP §

2164.01(a). The Factors most relevant to the instant rejection are addressed in detail

below.

The claims are overly broad in scope: As stated above, in view of the recitation of

at least, the claims are so broad as to encompass all polynucleotides consisting of at

least 15 contiguous nucleotides of SEQ ID NO:1. The broad scope of recited

polynucleotides are not limited to fragments of SEQ ID NO:1 and instead broadly

encompass polynucleotides that can be used as a PCR primer or hybridization probe for

a nucleic acid encoding any acyl-CoA synthase polypeptide. The scope of claimed

polynucleotides is not commensurate with the enablement provided by the disclosure

with regard to the extremely large number of polynucleotides broadly encompassed by

the claims. In this case the disclosure is limited to the isolated polynucleotide of SEQ ID

NO:1.

• The lack of guidance and working examples: The specification provides only a

single working example of the claimed polynucleotide, i.e., the polynucleotide of SEQ ID

NO:1. This working example fails to provide the necessary guidance for making the

entire scope of polynucleotides.

• The high degree of unpredictability in the art: The nucleotide sequence of an

encoding nucleic acid determines the corresponding encoded protein's structural and

functional properties. Predictability of which changes can be tolerated in a PCR primer

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Art Unit: 1652

or hybridization probe including nucleotide additions, deletions, and/or substitutions and obtain a nucleic acid by PCR or hybridization encoding polypeptide having the desired activity, *i.e.*, acyl-CoA synthase activity, is highly unpredictable.

- The state of the prior art supports the high degree of unpredictability: The state of the art provides evidence for the high degree of unpredictability in altering a polynucleotide sequence with an expectation that the encoded polypeptide will maintain the desired activity/utility. For example, Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York, 1991) teach "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design de novo stable proteins with specific functions" (page 247). As a representative example of the teachings of Branden et al., Witkowski et al. (Biochemistry 38:11643-11650) teaches that a single amino acid substitution results in conversion of the parent polypeptide's activity from a beta-ketoacyl synthase to a malonyl decarboxylase (see e.g., Table 1, page 11647). Thus, the prior art acknowledges the unpredictability of altering a proteinencoding sequence with an expectation of obtaining a protein having a desired function and discloses that even a single substitution in a polypeptide's amino acid sequence may completely alter the function of a polypeptide.
- The amount of experimentation required is undue: While methods of generating variants of a given polynucleotide and methods of isolating homologous polynucleotides

Art Unit: 1652

are known in the art, it is not routine in the art to screen for *all* polynucleotides as encompassed by claims 36-37.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high degree of unpredictability as evidenced by the prior art, and the amount of experimentation required to make and use the full scope of the claimed polynucleotides, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

## Biological Deposit

[15] It is noted that claims 30, 42, and 45 are drawn to a biological material, *i.e.*, a host cell comprising a novel vector having Accession Number DSM 13249. Applicants assert the claimed host cell has been deposited in accordance with the Budapest Treaty (see p. 18 of the specification). Further, applicants assert the host cell will be irrevocably

Art Unit: 1652

and without restriction or condition released to the public upon the issuance of a US patent (see p. 7 of the response filed May 12, 2003).

#### Citation of Relevant Art

[16] The art made of record and not relied upon is considered pertinent to applicant's disclosure. Pompejus et al. (US Patent 6,696,561) discloses a nucleic acid, SEQ ID NO:59, that encodes a polypeptide that is 100% identical to SEQ ID NO:2 (see Appendix A) and is 100% identical to nucleotides 159-2126 of SEQ ID NO:1 of the instant application (see Appendix B). Pompejus et al. claim domestic priority to US provisional application 60/141,031, filed June 25, 1999, which is before the effective US filing date of the instant application. However, the examiner can find no disclosure of the nucleic acid of SEQ ID NO:59 (denoted as RXA 00880) in provisional application 60/141,031. Applicants are advised that if SEQ ID NO:59 of Pompejus et al. is disclosed in the provisional application, Pompejus et al. may be applied as prior art against the pending claims.

#### Conclusion

## [17] Status of the claims:

- Claims 25-27 and 29-46 are pending.
- Claims 25-27, 29, 31-35, 40-41, and 43-44 appear to be in a condition for allowance.
- Claims 30, 36-39, 42, and 45-46 are rejected.

Art Unit: 1652

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 872-9306. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

10-27-04 David J. Steadman, Ph.D.

Primary Examiner Art Unit 1652

Art Unit: 1652

#### APPENDIX A

```
RESULT 1
AR477603
                                                   PAT 14-MAY-2004
                             1968 bp
                                      DNA
                                            linear
LOCUS
         AR477603
DEFINITION
         Sequence 59 from patent US 6696561.
         AR477603
ACCESSION
VERSION
         AR477603.1 GI:47235364
KEYWORDS
SOURCE
         Unknown.
 ORGANISM
         Unknown.
         Unclassified.
REFERENCE
         1 (bases 1 to 1968)
         Pompejus, M., Kroger, B., Schroder, H., Zelder, O. and Haberhauer, G.
 AUTHORS
         Corynebacterium glutamicum genes encoding proteins involved in
 TITLE
         membrane synthesis and membrane transport
         Patent: US 6696561-A 59 24-FEB-2004;
 JOURNAL
FEATURES
                Location/Qualifiers
                 1. .1968
    source
                 /organism="unknown"
                 /mol type="genomic DNA"
ORIGIN
Alignment Scores:
Pred. No.:
                   1.75e-206
                               Length:
                                           1968
                   3156.00
                               Matches:
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Score:
                               Conservative:
Percent Similarity:
                   100.00%
                                           1
Best Local Similarity:
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                               Mismatches:
                                           0
                                           0
Query Match:
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                               Indels:
                                           0
US-09-855-750A-2 (1-619) x AR477603 (1-1968)
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Qy
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Db
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Qу
           Db
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         41 TyrGlyValLeuPheSerLysProAlaAsnTyrGluTrpValAsnValThrAlaLysGlu 60
Qy
           TACGGAGTTTTGTTCAGCAAGCCTGCCAACTATGAGTGGGTGAATGTAACTGCCAAAGAA 268
Db
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Ov
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Db
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Qy
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Db
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Qy
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Qу
           TTGATGAAGAACCTGGTCATCGGTGAAGACGGAACTCCAGCGATTAAGGGTTCACCTTCC 568
Db
        161 LysLeuArgArgIleLeuGluIleAsnSerSerAlaLeuGluThrLeuLysPheGluGly 180
Qу
           569 AAGCTGCGCCGCATTCTAGAGATCAACTCTTCGGCGTTGGAGACCTTGAAGTTTGAGGGC 628
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Qу	201	AlaSerLeuValTyrThrSerGlyThrThrGlyArgProLysGlyCysGluLeuSerHis	220
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Qу		TyrHisTrpLeuAlaGluValArgAlaLeuIleThrAsnAspIleGlyAlaIleAlaMet	
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Qy Db		TTGGCCTTCGCTGTCACCGGTGCAACCCAGTCCCACTGGTCTGATTTCAGCACCCTTACT	
Qy		LeuGluLeuGlnArgSerArgProAsnLeuIleLeuGlyValProArgValPheGluLys	
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Qу	301	ValArgAsnAlaAlaAlaAlaAsnAlaAlaAspGlyGlyAlaIleLysArgIleMetPhe	320
Db	989	GTCCGCAACGCCGCTGCTAATGCTGCTGACGGTGGCGCAATCAAGCGCATCATGTTT	1048
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Qу	341	SerLysSerGlnValMetAlaHisLysAlaPheAspLysLeuValTyrSerLysIleArg	360
Db	1109	AGCAAGTCCCAGGTTATGGCACATAAAGCGTTTGACAAGCTGGTGTACTCCAAGATCCGT	1168
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QУ		LeuLeuHisPhePheArgGlyValGlyMetThrIleTyrGluGlyTyrGlyLeuThrGlu	
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Qy Db		TCTGCGGCTGCTGCAGCGGTGGACTTCACTGATCAAAAGATCGGCACTGTGGGTAAGCCG	
Qу		MetGlyGlyMetThrIleLysIleAsnGluAspGlyGluIleMetLeuLysGlyGluMet	
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Qу	441	LeuPheGlnGlyTyrTrpAsnAsnProGluAlaThrAlaGluAlaLeuHisAspGlyTrp	460
Db	1409		1468
Qу	461	PheAsnThrGlyAspLeuGlyGluLeuLeuGluSerGlyHisLeuValIleThrGlyArg	480
Db	1469	TTCAACACCGGCGATCTGGAGCTGTTGGAGTCTGGACACCTGGTGATCACCGGACGT	1528
Qу	481	LysLysAspLeuIleValThrAlaGlyGlyLysAsnValSerProGlyProMetGluAsp	500
Db	1529	${\tt AAGAAAGATCTGATCGTGACCGCGGGCGGCAAGAACGTTTCCCCAGGACCCATGGAAGAC}$	1588
Qу	501	IleIleArgAlaHisProLeuValSerGlnAlaMetValValGlyAspGlyLysProPhe	520

Db	1589	ATCATCCGCGCACACCCACTGGTCAGCCAGGCCATGGTGGTGGGCGATGGTAAACCATTC	1648
Qy	521	ValGlyLeuLeuValThrLeuAspProAspMetLeuLysArgTrpLysLeuAsnHisAsn	540
Db	1649	GTTGGCCTGCTGGTCACCTTGGATCCAGATATGTTGAAGCGGTGGAAGCTGAACCACAAC	1708
Qy	541	IleAlaGluSerArgThrValSerGluIleAlaThrAspProAlaLeuArgAlaGluIle	560
Db	1709	ATTGCGGAATCCCGCACGGTTTCTGAGATTGCTACTGATCCTGCACTGCGTGCG	1768
Qy	561	GlnAspAlaValAsnAsnAlaAsnAlaThrValSerHisSerGluAlaIleLysArgPhe	580
Db	1769		1828
Qy	581	TyrIleLeuAspArgAspLeuThrGluGluAlaAspGluLeuThrProThrLeuLysVal	600
Db	1829		1888
Qy	601	LysArgAsnValValValArgArgTyrAlaAspAlaIleAspHisIleTyrAsnArg 619	7
Db	1889		15

Art Unit: 1652

#### **APPENDIX B**

Οv

```
RESULT 8
AR477603
                                               PAT 14-MAY-2004
LOCUS
        AR477603
                          1968 bp
                                  DNA
                                        linear
DEFINITION
        Sequence 59 from patent US 6696561.
ACCESSION
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VERSION
        AR477603.1 GI:47235364
KEYWORDS
SOURCE
        Unknown.
 ORGANISM
        Unknown.
        Unclassified.
REFERENCE
        1 (bases 1 to 1968)
        Pompejus, M., Kroger, B., Schroder, H., Zelder, O. and Haberhauer, G
 AUTHORS
 TITLE
        Corynebacterium glutamicum genes encoding proteins involved in
        membrane synthesis and membrane transport
 JOURNAL
        Patent: US 6696561-A 59 24-FEB-2004;
FEATURES
               Location/Qualifiers
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               1. .1968
               /organism="unknown"
               /mol type="genomic DNA"
ORIGIN
                   85.6%; Score 1968; DB 6; Length 1968;
 Best Local Similarity
                  100.0%; Pred. No. 0;
 Matches 1968; Conservative
                        0; Mismatches
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       159 TCCATGTGGTTAAAGATATGCCTAAAGATCTGACCAAAAACGTGACTAAAGACGTGACGA 218
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          Db
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Qу
          Db
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       459 AATTATTTCAGTCGGCGTAGAGCAGGGAGACCGTGTCGCGCTGCTGTCCAATACTCGCTA 518
Qу
          Db
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Qу
          Db
       361 TGAGTGGGCTGTGCTTGATTTCGCTATCTGGGCCGCTGGCGCAGTGAGCGTGCCTATCTA 420
       579 CAGCTCCTCTCACTGTCCCAAATTGAGTGGATCATTGAGGATTCCGGCGCTGTTTTGGC 638
Oν
          Db
          CAGCTCCTCTTCACTGTCCCAAATTGAGTGGATCATTGAGGATTCCGGCGCTGTTTTGGC 480
Qу
       639 CATTACCGAAACCCCTGATCATACCGACTTGATGAAGAACCTGGTCATCGGTGAAGACGG 698
          Db
       481 CATTACCGAAACCCCTGATCATACCGACTTGATGAAGAACCTGGTCATCGGTGAAGACGC 540
          AACTCCAGCGATTAAGGGTTCACCTTCCAAGCTGCGCCGCATTCTAGAGATCAACTCTTC 758
Qу
          AACTCCAGCGATTAAGGGTTCACCTTCCAAGCTGCGCCGCATTCTAGAGATCAACTCTTC 600
Db
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759 GGCGTTGGAGACCTTGAAGTTTGAGGGCCGCGAGCTTTCTGATGAGCTGGTGTGGGAACG 818

		- [ ]   ]	
Db	601		660
Qy	819	CATTCATGCAACCAAGGCCGCTGACCTGGCGTCTTTGGTGTACACCTCTGGCACAACTGG	878
Db	661	${\tt CATTCATGCAACCAAGGCCGCTGACCTGGCGTCTTTGGTGTACACCTCTGGCACAACTGG}$	720
Qy	879	TAGGCCGAAGGGCTGCGAGTTGTCCCACTACCACTGGTTGGCTGAGGTCCGAGCGCTGAT	938
Db	721	TAGGCCGAAGGGCTGCGAGTTGTCCCACTACCACTGGTTGGCTGAGGTCCGAGCGCTGAT	780
Qy	939	CACCAATGACATCGGAGCGATCGCGATGCCAGGTTCAAGGTTGCTCACCTTCCTT	998
Db	781	CACCAATGACATCGGAGCGATCGCGATGCCAGGTTCAAGGTTGCTCACCTTCCTT	840
Qу	999	GGCGCACGTTCTTGCTCGCGCAGTGCACTTGGCCTTCGCCGTTCACCGGTGCAACCCAGTC	1058
Db	841	${\tt GGCGCACGTTCTTGCTCGCGCAGTGCACTTGGCCTTCGCTGTCACCGGTGCAACCCAGTC}$	900
Qy		CCACTGGTCTGATTTCAGCACCCTTACTTTGGAACTGCAGCGTTCCCGCCCG	
Db		${\tt CCACTGGTCTGATTTCAGCACCCTTACTTTGGAACTGCAGCGTTCCCGCCCG$	
Qy .		TTTGGGTGTTCCACGCGTGTTTGAAAAGGTCCGCAACGCCGCTGCTGCTAATGCTGCTGA	
Db		TTTGGGTGTTCCACGCGTGTTTGAAAAGGTCCGCAACGCCGCTGCTGCTAATGCTGCTGA	
Qy Db		CGGTGGCGCATCAAGCGCATCATGTTTGAGCGTGCCGAAAAGGCGGCCATTGAATACTC	
_		CATGGCTCTTGATACTGCAGAAGGCCCAAGCAAGTCCCAGGTTATGGCACATAAAGCGTT	
Qу Db		CATGGCTCTTGATACTGCAGAAGGCCCAAGCAAGTCCCAGGTTATGGCACATAAAGCGTT	
Qy		TGACAAGCTGGTGTACTCCAAGATCCGTGCAGCTGTCGGTGGCGATGTGCAGTACGCCAT	
Db			
Qу	1359	CACCGGTGGTTCAGCGATGGGGCAGGAGCTGCTGCACTTCTTCCGCGGTGTGGGCATGAC	1418
Db	1201		1260
Qу	1419	${\tt CATCTACGAAGGTTATGGTCTGACGGAATCTGCGGCTGCTGCAGCGGTGGACTTCACTGA}$	1478
Db	1261		1320
Qy	1479	TCAAAAGATCGGCACTGTGGGTAAGCCGATGGGTGGCATGACCATCAAGATCAATGAAGA	1538
Db	1321	TCAAAAGATCGGCACTGTGGGTAAGCCGATGGGTGGCATGACCATCAAGATCAATGAAGA	1380
QУ	1539	TGGCGAAATCATGCTAAAAGGCGAGATGTTGTTCCAGGGATATTGGAACAACCCAGAAGC	1598
Db	1381	TGGCGAAATCATGCTAAAAGGCGAGATGTTGTTCCAGGGATATTGGAACAACCCAGAAGC	1440
Qу	1599	CACAGCAGAAGCCCTCCACGACGGTTGGTTCAACACCGGCGATCTGGGTGAGCTGTTGGA	1658
Dp ,	1441	CACAGCAGAAGCCCTCCACGACGGTTGGTTCAACACCGGCGATCTGGGTGAGCTGTTGGA	1500
Qy	1659	GTCTGGACACCTGGTGATCACCGGACGTAAGAAAGATCTGATCGTGACCGCGGGCGG	1718
Db	1501	GTCTGGACACCTGGTGATCACCGGACGTAAGAAAGATCTGATCGTGACCGCGGGCGG	1560
Qу	1719	GAACGTTTCCCCAGGACCCATGGAAGACATCATCCGCGCACACCCACTGGTCAGCCAGGC	1778
Db	1561	${\tt GAACGTTTCCCCAGGACCCATGGAAGACATCATCCGCGCACACCCACTGGTCAGCCAGGC}$	1620

Qу	1779	CATGGTGGTGGTGGTAAACCATTCGTTGGCCTGCTGGTGACCTTGGATCCAGATAT	1838
Db	1621		1680
Qy	1839	GTTGAAGCGGTGGAAGCTGAACCACAACATTGCGGAATCCCGCACGGTTTCTGAGATTGĆ	1898
Db	1681	GTTGAAGCGGTGGAACCACAACATTGCGGAATCCCGCACGGTTTCTGAGATTGC	1740
Qy	1899	TACTGATCCTGCACTGCGTGCGGAAATCCAGGATGCAGTCAACAACGCTAATGCCACGGT	1958
Db	1741	${\tt TACTGATCCTGCACTGCGTGCGGAAATCCAGGATGCAGTCAACAACGCTAATGCCACGGT}$	1800
Qy	1959	GTCTCATTCAGAGGCGATCAAGCGGTTCTACATCCTTGATCGCGACCTGACCGAGGAAGC	2018
Db	1801	GTCTCATTCAGAGGCGATCAAGCGGTTCTACATCCTTGATCGCGACCTGACCGAGGAAGC	1860
Qy	2019	CGACGAGCTGACCCCAACGCTGAAGGTCAAGCGCAACGTTGTTGTTCGCCGTTACGCAGA	2078
Db	1861	$\tt CGACGAGCTGACGCTGAAGGTCAAGCGCAACGTTGTTGTTCGCCGTTACGCAGA$	1920
Qy	2079	CGCCATCGACCACATCTACAACCGATGAGTAACACAGAGACCCAATTT 2126	
Db	1921	CGCCATCGACCACATCTACAACCGATGAGTAACACAGAGACCCAATTT 1968	